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Significant genetic association of a functional TFPI variant with circulating fibrinogen levels and coronary artery disease

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The tissue factor pathway inhibitor (TFPI) gene encodes a protease inhibitor with a major role in regulation of blood coagulation. In this project, we performed a large population-based study with 2,313 study subjects for which blood coagulation data are available, including the Fg level, the PT level, the APTT level and the TT level. We selected a functional variant in the promoter of TFPI, rs10931292, which was found to reduce the transcription of TFPI and genotype it in the 2,313 study subjects using the TaqMan assay. We carried out the linear regression analysis under three different genetic models, including an additive model, an autosomal dominant model or an autosomal recessive model, for the genotyping data. Our analysis identified significant association of TFPI variant rs10931292 with increased plasma Fg levels (P=0.017 under a recessive model), but not with PT, APTT or TT (P>0.05). To the best of our knowledge, this is the first time to show that a TFPI variant is significantly associated with plasma Fg levels. These data identify a novel genetic variant for Fg levels and contributes importantly to the elucidation of the genetic basis and biological pathways for plasma Fg levels. An increased plasma Fg level is a well-established risk factor for cardiovascular disease. Therefore, we determined whether TFPI SNP rs10931292 was also associated with risk of CAD. Using a large case control association study population with 4,479 CAD patients and 3,628 controls, we identified significant association between TFPI SNP rs10931292 and CAD under a recessive genetic model (OR = 1.23, P = 0.005). Individuals with the GG/CC genotype had a significantly increased risk of CAD (OR = 1.23, P = 0.005). These data identify a new genetic variant that increases risk of CAD and contributes importantly to the elucidation of the genetic basis and biological pathways for the pathogenesis of CAD.

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